SYNTHESIS OF ALKOXYETHYLINDOLES

G. G. Skvortsova, E. S. Domnina, and N. P. Glazkova

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 2, pp. 255–257, 1969

UDC 547.752:543.422.4

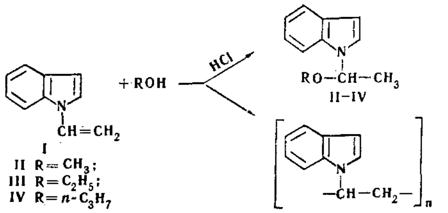
In the reaction of N-vinylindole with alcohol, two reactions compete: the addition of the alcohol and homopolymerization. N-(α-alkoxyethyl) indoles have been obtained for the first time. In the reaction of N-vinylindole with monocarboxylic acids, only homopolymerization takes place.

Information in the literature on the reaction of N-vinyl compounds with alcohols is very limited. It is known that N-vinylpyrrolidone adds aliphatic alcohols to the double bond of the vinyl group at room temperature in the presence of hydrogen chloride with the formation of alkoxyethylidenepyrrolidones [1]. According to patent information, similar products are obtained by the action of phenols on N-vinyllactams [2, 3].

This paper is devoted to the question, which has not been previously studied, of the reaction of N-vinylindole (I) with hydroxyl-containing compounds.

Calculation of the electronic structure of the molecule of I by means of the semiempirical SCF MO LCAO method leads to high values of the π-electron density on the β-carbon atom of the vinyl group [4]. This permitted us to assume that the addition of alcohols to I should take place in accordance with Markovnikov's rule.

The reactions of I with methanol, ethanol, propanol, and butanol, and also with phenol, were studied. It was found that in these cases there are two competing reactions. Under the influence of acid catalysts, not only does the alcohol add to I at the double bond of the vinyl group, but the I also polymerizes:



Depending on the temperature conditions of the reaction, the order of addition of the reactants, and the nature of the hydroxyl-containing compound, one direction of the process or the other predominates. If the reaction is carried out at room temperature, by analogy with N-vinylpyrrolidone, in the presence of catalytic amounts of HCl in an alcoholic medium only the homopolymerization of I takes place, and the second reactant does not take part in an addition reaction and is recovered quantitatively when the reaction mixture is distilled. Methanol and ethanol are capable of reacting with I under exceptionally mild conditions reducing the possibility of its polymerization to a minimum.

Thus, the reaction between methanol and I takes place at temperatures below 0° C. The yield of N-(α-methoxyethyl)indole (II) amounts to 66%. Ethanol reacts with I at 0° C to form N-(α-ethoxyethyl)indole (III) with a yield of 74%. A slight rise in the temperature—for example to 3–5° C—leads to a marked decrease in the yield of addition product (to about 15–17%). With an increase in the molecular weight of the alcohol, its activity in addition to I falls. We succeeded in synthesizing N-(α-propoxyethyl)indole (IV) with a yield of only 18%, the remainder of the initial I being converted mainly into polymer. It was impossible to obtain an addition product with n-butanol or phenol, since I polymerizes quantitatively in an acid medium at temperatures close to room temperature and above [4].

An attempt to obtain N-(α-butoxyethyl)indole indirectly by the action of butyl vinyl ether on indole was also unsuccessful.

The correctness of the structure of N-(α-alkoxyethyl)indoles synthesized was shown refractometrically, by a study of their IR spectra, and also by their hydrolytic decomposition. In the IR spectrum of N-(α-methoxyethyl)indole, there are bands with frequencies in the 3050 cm^{-1} and 1620–1520 cm^{-1} regions that are characteristic for the indole ring and bands at 1060–1150 cm^{-1} corresponding to the asymetric stretching vibrations of the C—O—C group. In the addition product, the band at 1640 cm^{-1} had disappeared and there was absorption at 2940 cm^{-1}, which is apparently due to the presence of the methyl group in the ethylidene radical [5].

A confirmation of the addition of alcohols to I in accordance with Markovnikov's rule is the fact that all the compounds obtained hydrolyze under the action of dilute sulfuric acid at 40° C with the formation of acetaldehyde, indole, and the corresponding alcohol.

The N-(α-alkoxyethyl)indoles are high-boiling oily liquids decomposing on distillation under atmospheric pressure, stable on storage, and soluble in acetone, ethanol, and ether.

Our experimental investigations carried out with the aim of obtaining products of the addition of monocarboxylic acids to I were unsuccessful. In spite of a wide variation in the reaction conditions, it was impossible to effect the acylation of I at the double band of the vinyl group with such acids as formic, acetic, butyric, isobutyric, and valeric. The I polymerized instantaneously or in the course of several hours, according to the strength of the initial acid.

EXPERIMENTAL

N-(α-Methoxyethyl)indole (II). A solution of 1 g (7 mM) of I in 15 ml of ethanol was added over 2 hr to a solution of 0.3 g (9.4 mM) of absolute methanol in 15 ml of acetone with the addition of two drops of hydrochloric acid at −8° C. After 30 min, the reaction mixture was neutralized with potassium carbonate. The solvent and unchanged methanol were distilled off, and vacuum distillation of the residue yielded 0.8 g (66%) of **II**, bp 95° C (2 mm); (n_D^{20} 1.5635; d_4^{20} 1.0593). Found, %: C 75.47; H 7.46; N 8.12; MR_D 53.67. Calculated for ($C_{11}H_{13}NO$), %: C 75.42; H 7.42; N 8.00; MR_D 53.68.

N-(α-Ethoxyethyl)indole (III). A solution of 2.2 g (15 mM) of I in 30 ml of acetone was added over 3 hr 30 min to a solution of 2 g (43 mM) of absolute ethanol in 10 ml of acetone containing two drops of hydrochloric acid at 0° C. After neutralization with potassium carbonate, vacuum distillation yielded 2.2 g (74%) of **III**, bp 115° C (3 mm); (n_D^{20} 1.5600; d_4^{20} 1.0382). Found, %: C 76.81; H 7.93; N 7.18; MR_D 58.85. Calculated for ($C_{12}H_{15}NO$), %: C 76.16; H 7.46; N 7.40; MR_D 58.29.

A mixture of 0.83 g of III and 20 ml of 0.5% H_2SO_4 was heated in a sealed tube at 40° C in an atmosphere of nitrogen for 6 hr and was then poured into a cooled solution of 2, 4-dinitrophenylhydrazine to yield 0.2 g of acetaldehyde 2, 4-dinitrophenylhydrazone, mp 145–146° C [6].

N-(α-Propoxyethyl)indole (IV). A solution of 1.9 g (13 mM) of I in 10 ml of acetone was added over 2 hr to a mixture of 1.3 g (22 mM) of n-propanol in 20 ml of acetone containing two drops of hydrochloric acid at 3–5° C. After neutralization with potassium carbonate, vacuum distillation yielded 0.6 g (18.7%) of **IV**, bp 145° C (3 mm); (n_D^{20} 1.5458; d_4^{20} 1.0191). Found, %: C 76.80; H 8.26; N 6.47; MR_D 63.04. Calculated for ($C_{13}H_{17}NO$), %: C 76.81; H 8.43; N 6.88; MR_D 62.91. The residue after vacuum distillation was dissolved in 2 ml of acetone and precipitated with 50 ml of ethanol. This gave 0.96 g of poly(vinylindole), mp 185–216° C. Found, %: N 9.58. Calculated for $(C_{10}H_9N)_n$, %: N 9.79.

REFERENCES

1. M. F. Shostakovskii, F. P. Sidel'kovskaya, M. G. Zelenskaya, T. N. Shkurina, and T. Ya. Ogibina, Izv. AN SSSR. OKhN, 482, 1961.
2. German patent no. 743945, 1940.
3. German patent no. 851197, 1952.
4. M. F. Shostakovskii, G. G. Skvortsova, E. S. Domnina, and Yu. L. Frolov, DAN, Ser. khim. nauk, 593, 1967.
5. K. Nakanishi, Infrared Absorption Spectroscopy [Russian translation], Mir, Moscow, pp. 42, 64, 1965.
6. I. Heilbron and H. M. Bunbury, Dictionary of Organic Compounds, Vol. 1 [Russian translation], IL, Moscow, p. 4, 1949.

15 November 1966

Irkutsk Institute of Organic
Chemistry, Siberian Division AS USSR